reabsorptive capacity varies with short-term changes in Pi supply. We also studied if it varies with a short-term variation of a Pi requirement, which can be expected to occur during fasting. Using clearance methodology we studied the influence of overnight fasting on the tubular capacity to reabsorb Pi in rats. Fasted animals were or were not supplemented with Pi in amounts corresponding to those absorbed by the fed group. This protocol allowed us to dissociate the effect of overnight fasting *per se* from that of overnight Pi deprivation. Tubular Pi reabsorptive capacity was found to be lower in overnight fasted animals receiving a Pi supplement in the drinking water than in fed animals. In overnight fasting rats it was lower in animals receiving a Pi supplement in the drinking water than in those without Pi supplement. There was no difference in tubular Pi reabsorptive capacity between completely fasted and fed rats. These results indicate that overnight fasting with constant Pi supply decreases the tubular reabsorptive capacity for Pi, whereas overnight Pi deprivation stimulates it. These two opposite effects explain the fact that overnight fasting without Pi supplement has no significant influence on tubular Pi transport capacity. Furthermore, these results show that the kidney can adapt its transport capacity for Pi according to short-term changes in Pi supply and requirement, that is in less than 14 hours.

Double-blind comparison of three antihypertensive drugs by internists in private practice. *B. Waeber, H. R. Brunner, R. K. Ferguson, G. A. Turini, H. Gavras. Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.* The antihypertensive effects of debrisoquine, methyldopa, and propranolol were studied in a double-blind fashion by 14 internists in practice. An open phase of 6 weeks during which treatment consisted only of a diuretic (mefruside, 25 mg/day), was followed by four treatment periods of 4 weeks each in randomized sequence consisting of placebo, debrisoquine (20 mg/day), methyldopa (1000 mg/day), or propranolol (160 mg/day). Mefruside was continued at the same dose. At the end of the open phase, the blood pressure of 48 patients with essential hypertension remained elevated at 168/111 ± 20/14 mm Hg (mean ± SD). A significant fall in blood pressure was achieved not only at the end of active treatments but also after administration of placebo with the blood pressure reaching 160/103 ± 20/11 mm Hg. Compared with placebo, blood pressure was significantly lower during the active medication periods. However, the comparative fall for systolic blood pressure ranged only from 6 (debrisoquine) to 12 (methyldopa) mm Hg and for diastolic from 4 (debrisoquine) to 5 mm Hg (methyldopa, propranolol), with no significant difference appearing between active drugs. Propranolol was slightly better tolerated than the others. After the study period, antihypertensive therapy at the choice of the internist was continued in 36 patients. In these patients, with free choice of medication the drop in blood pressure averaged 10/9 mm Hg. *Conclusions.* In the hands of practicing internists, the antihypertensive efficacy of debrisoquine, methyldopa, and propranolol is essentially equal. However, at the doses used they were only slightly more effective than placebo. Not surprisingly, internists in practice are able to obtain better antihypertensive results when allowed free choice of medication.

Chloride reabsorption in various conditions of hypokalemia in man. *G. Williams, L. Favre, G. Lucot, H. Favre, and M. B. Vallotton. Divisions d'Endocrinologie et de Néphrologie, Hôpital Cantonal, Genève, Switzerland.* Because a defect in chloride transport has been proposed as a specific cause of Bartter's syndrome, the relationship between fractional distal delivery of chloride (FDD_{Cl}) and fractional reabsorption of chloride (FDR_{Cl}) was studied in 8 patients with potassium depletion, by using clearance techniques under maximal water diuresis. Two patients had all the characteristics of Bartter's syndrome; despite chronic treatment with indomethacin, hypokalemia was still present (plasma K, 2.2 and 2.3 mmoles/liter). Among the 6 other K-depleted patients (plasma K, 1.7 to 3.4 mmoles/liter), there were 2 cases of psychogenic vomiting, 2 laxative abusers, 1 case of anorexia nervosa, and 1 experimental subject given a low-K diet and cation exchange resin. For the 6 latter patients, FDR_{Cl} was positively correlated with inulin clearance ($r = 0.63$, $P < 0.05$), and inversely correlated with FDD_{Cl} ($r = -0.94$, $P < 0.001$), but completely unrelated to plasma K. In the 2 patients with Bartter's syndrome, FDR_{Cl} was slightly lower than expected from the latter regression (0.63 and 0.72, c.f. predicted 0.85 and 0.87). However, these 2 values were similar to those observed in 2 other hypokalemic patients having decreased inulin clearance and increased FDD_{Cl} without Bartter's syndrome. As the 2 cases of Bartter's syndrome had normal inulin clearance, the effect of low GFR on FDR_{Cl} could not be evaluated in this syndrome. After withdrawing indomethacin in one of the 2 cases, FDR_{Cl} remained unchanged, suggesting that prostaglandins do not affect chloride reabsorption. Thus, a reduced FDR_{Cl} may well be a feature of Bartter's syndrome, but may also be found in various conditions of potassium depletion associated with renal failure, and consequently it cannot be used as a specific diagnostic criterium.

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Ticrynafen (tienilic acid), a uricosuric diuretic drug. *G. G. Geyskes, B. B. A. Laemers, J. J. M. van Bussel, P. Boer, and E. J. Dorhout Mees. Department of Nephrology and Hypertension, University Hospital, Utrecht, The Netherlands.* In 24 patients with essential hypertension (as defined by the World Health Organization as stages I and II) whose blood pressure remained > 130/90 during chronic atenolol treatment, the effects of adding 250 mg of ticrynafen (TCN) or 50 mg of chlortalidone (CHT) were investigated in a double-blind crossover study. Serum uric acid decreased during TCN and increased during CHT; CHT also increased serum cholesterol concentration. As compared to CHT, TCN caused less blood pressure reduction and less volume depletion (as measured by body weight and plasma renin activity).

When CHT was replaced by TCN, the average urinary creatinine excretion of all patients was significantly lower on the first day of TCN following CHT as compared to the preceding day on CHT, but not on the first day TCN after placebo. One patient complained of loin tenderness and showed diminished urine production on the first day TCN directly following CHT in the preceding period. Blood studies revealed a renal insufficiency that improved gradually after discontinuation of TCN. To study the effect of replacing chronic CHT by TCN in more detail, we performed a study in five hospitalized patients, also with essential

	Day 0	Day 1	Day 2	Day 5	Day 14	Day 28
Patient 1						
chlortalidone, *mg*	50					
ticrynafen, *mg*		250	250	250	250	250
serum urea, *mmoles/liter*	12.6	21.3	27.1		17.0	17.1
serum creatinine, *μmoles/liter*	170	355	410		180	185
diuresis, *ml/day*	2275	1370	2865			
Patient 2						
chlortalidone, *mg*	50					
ticrynafen, *mg*		250	250			
serum urea, *mmoles/liter*	7.4	17.5	23.2	41.0	16.4	6.3
serum creatinine, *μmoles/liter*	70	300	515	690	140	100
diuresis, *ml/day*	1175	72	80	1570	1840	
Patient 3						
chlortalidone, *mg*	100					
ticrynafen, *mg*		500	500			
serum urea, *mmoles/liter*	7.7	16.2	20.8	32.0	12.9	8.1
serum creatinine, *μmoles/liter*	90	355	530	800	200	115
diuresis, *ml/day*	1060	280	807	1660	1960	

hypertension. One patient developed a moderate renal insufficiency on the first day of TCN that was reversible during continued TCN treatment. Two other patients developed frank oliguria on the first day of TCN; TCN was discontinued; the increase of blood urea and creatinine was maximal on day 5 and returned to normal pretreatment values in the following 3 weeks (see Table 1). The high frequency of this renal complication in the first day on TCN, following chronic CHT therapy, but not after placebo, points to a possible interaction of the two drugs. The exact nature of the renal insufficiency is not known. Uric acid nephropathy seems unlikely because the uric acid excretion in the first urine samples during TCN was not high, and no uric acid crystal were seen. Renal insufficiency during TCN after preceding CHT therapy is a frequently occurring serious complication. It warrants caution during more general use of this otherwise valuable drug.

Effects of oral converting enzyme inhibitor, Captopril, on renin and blood pressure in renovascular hypertension and anephric subjects. *J. H. B. de Bruyn, A. J. Man in 't Veld, G. J. Wenting, F. H. M. Derkx, I. M. Schicht, and M. A. D. H. Schalekamp. Department of Internal Medicine I, University Hospital Dijkzigt, Rotterdam and Department of Nephrology, University Hospital Leiden, Leiden, The Netherlands.* The renin-angiotensin (RA) system and kallikrein-kinin (KK) system share the enzyme, kininase II converting enzyme. Until now the blood pressure drop after converting enzyme inhibition with Captopril (C) has been claimed to be caused by falling levels of circulating angiotensin II. In anephric subjects, 2 hours after fluid withdrawal during heamodialysis, causes a significant drop in blood pressure in contrast to placebo. This fall in blood pressure is maximal after 24 hours and even more pronounced on standing, orthostatic hypotension developing in all patients. After fluid repletion, C had no effect on blood pressure in these patients. Renin is very low in these patients, so the blood pressure drop can not be accounted for by changes in circulating angiotensin II alone. Another connection between the RA system and the KK system is seen in the process of activation of inactive plasma renin (IR) in vitro. After acid-treatment, IR is converted at pH 7.5 into active renin (AR). This activation at pH 7.5 can be blocked by adding Trasylol®. So, this activation of IR is caused by an endogenous serine protease. Exogenous serine proteases such as trypsin are equally effective in activating IR at pH 7.5. In prekallikrein (Fletcher factor) -deficient plasma as well as in factor-XII (Hagemen factor) -deficient plasma, acid activation of IR does not occur, in contrast with activation of IR by trypsin. In plasma, activation of prekallikrein is caused by factor XII. Adding active kallikrein to factor-XII-deficient plasma caused activation of IR to values not different from trypsin treatment. Adding active factor XII to prekallikrein-deficient plasma had no effect. So plasma kallikrein is the major endogenous activator of IR in vivo. After nephrectomy IR falls to values not different from those seen in low-renin essential hypertension (LHT). After C, IR rises in LHT; in anephric subjects IR does not change. So IR has an important extrarenal source. The presence of the kidney, however, is essential for changes in IR after stimulation. In patients with unilateral renal artery stenosis, levels of IR in renal artery and renal vein on the affected side are not different. After stimulation by C, IR in the renal vein fell to levels far below those in the renal artery. In contrast, AR in the renal vein rose markedly. These opposite changes in AR and IR suggest activation of IR in vivo. Whether kallikrein plays a role in this activation process in vivo or not is not clear. In vitro experiments during acid activation of IR and prekallikrein show that almost all IR is activated, as prekallikrein levels have fallen by less than 10%. So the possible changes of plasma prekallikrein and kallikrein during activation of IR in vivo will be small and hardly demonstrable.

Renal vascular tachyphylaxis to angiotensin II in the dog: Specificity and the role of prostaglandins and bradykinin. *P. W. de Leeuw, L. G. Meggs, N. K. Hollenberg, and W. H. Birkenhäger. Department of Medicine and Radiology, Peter Bent Brigham Hospital and Harvard Medical School, Boston, Massachusetts, USA and Department of Medicine, Zuiderziekenhuis, Rotterdam, The Netherlands.* A hypothesis concerning angiotensin's role in sustained renal vasoconstriction must account for the rapid development of tachyphylaxis to angiotensin II (AII). Data from the literature suggest that prostaglandins (PG's) may be involved in this process. Because these could act either by receptor modulation or by nonspecific vasodilation, we studied the effect of AII and norepinephrine (NE) on the renal vasculature (electromagnetic flow meter) in the anesthetized dog. In a first series of experiments (6 dogs), tachyphylaxis to AII infused into the renal artery was demonstrated within 10 min. The response to NE was well-maintained at that time, but disappeared in some dogs with prolonged infusion. In another group of 7 dogs, we found that PGE_1, in a dose that increased renal blood flow by 30% did not modify the response to bolus injections of AII or NE. Equivalent doses of PGE_2 (5 dogs), $PGF_{2\alpha}$ (6 dogs), and PGI_2 (7 dogs) showed similar results. Infusion of bradykinin (BK), however, completely abolished and even reversed the response to AII and NE (10 dogs). We conclude that specific desensitization to AII (tachyphylaxis) may be followed by a nonspecific offsetting vasodilating mechanism. If PG's are involved in AII tachyphylaxis, and as yet not identified PG must be the mediator. Endogenous BK may serve as a modulator of renal vascular tone and reactivity.

Anti-T-cell specificity in nephritogenic antibodies. *W. W. Bakker, W. M. Bagchus, J. T. W. M. Vos, K. Kooistra, and Ph. J. Hoedemaeker. Department of Pathology, State University of Groningen, Groningen, The Netherlands.* Injection of rats with rabbit antibodies against the brushborder (BB) of proximal tubules of the rat kidney results in immediate immune complex formation along the epithelial side of the glomerular basement membrane (GBM). Previous experiments suggested that these anti-BB antibodies also possess an in vitro cytotoxic activity against rat thymocytes. We have compared the specificities of anti-BB antibodies with antirat thymocytes (anti-THY) antibodies using direct migration inhibition assays, as well as a cytotoxicity assay on thymocytes using guinea pig serum as complement source. Immunofluorescent studies with these sera were performed on normal frozen kidney sections, and absorption studies were carried out using the BB antigen, thymocyte, and brain extracts; the latter extracts were used as thymocyte membrane (THY) antigens. (Thymocyte membrane antigens are referred to as Thy, which is not identical to the purified Thy-1 antigen in the rat, although this material contains probably much Thy-1 antigen, which is present in considerable amounts in rat brain and thymus cells.)

The results indicate that *(1)* anti-BB as well as anti-THY antibodies are able to stain brushborders in frozen kidney sections. This staining can be abolished by absorption of the antisera with BB antigen but not with THY antigens. *(2)* Both anti-BB and anti-THY antibodies can induce a dose-related migration inhibition of thymocytes. These activities of either anti-BB or anti-THY antibodies can be inactivated after absorption to their respective antigens. Absorption with THY antigen removes, however, the activity from anti-BB sera partially, as does absorption with BB-antigen of anti-THY antisera. *(3)* Both anti-BB antibodies and anti-THY antibodies are cytotoxic for rat thymocytes in vitro. The cytotoxicity of anti-BB antibody can be absorbed with both BB and THY antigens. Cytotoxicity of anti-THY antisera can be absorbed, however, only with THY antigens. Absorption with BB antigens only reduces partially this cytotoxic activity. From these results, we concluded that anti-BB antibodies contain at least two specificities: one directed against BB antigens and one directed against THY antigens. One the other hand, anti-THY antibodies contain mainly antibodies directed against THY antigens and to a lesser extent to BB antigens. The findings of this study indicate some relation exists between BB and THY antigens, which might be important in the pathogenesis of experimental autologous and heterologous immune complex glomerulopathy, especially in view of recent concepts on in situ formation of immune complexes in this type of experimental disease.

Triple drug treatment of autologous immune complex glomerulonephritis. *G. J. Fleuren and P. J. Hoedemaeker. Deparment of Pathology, Groningen, The Netherlands.* Autologous immune complex glomerulonephritis (AIC), an established experimental model of membranous glomerulopathy in man, which is induced in rats through immunization with renal tubular antigens (Fx1A), has been used to investigate the effect of various drugs on its course. Because immunosuppressive or anti-inflammatory drugs were reported to have little or no effect on AIC, a combination of cyclophosphamide, azathioprine, and prednisolone (triple drug) was used in this study. Because we previously reported that AIC probably results from binding of free-circulating anti-Fx1A antibody to antigens present in the glomerular basement membrane (GBM), special attention was paid to the effect of triple drug treatment on the anti-Fx1A serum titers and the relation between these titers, deposition of immune aggregates along the GBM, and the occurrence of proteinuria. It was found that triple-drug treatment consisting of 9 mg/kg cyclophosphamide, 9 mg/kg azathioprine, and 3.6 mg/kg prednisolone, given three times a week simultaneously with the immunization procedure, could completely prevent formation of anti-Fx1A antibody and deposition of immune aggregates in the glomeruli, as well as development of proteinuria. It triple-drug treatment was injected daily during 6 weeks from week 9 onwards, a moment when immune deposits were present along the GBM but proteinuria had not yet developed, a decrease in serum titers of anti-Fx1A antibody, diminished deposition of immune aggregates along the GBM, and a significant decrease of proteinuria were found. In later stages of the disease, when proteinuria was developed, no beneficial effect of triple-drug treatment could be demonstrated. Proteinuria persisted in these rats, although complement was not present anymore along the GBM, which indicates that proteinuria in later stages of AIC is independent of complement binding. We conclude that the beneficial effect of triple-drug treatment in early stages of AIC is caused by a decrease in the level of free-circulating anti-Fx1A antibody. The lack of benifit in later stages of AIC probably can be explained by the fact that proteinuria in these stages results from structural damage of the GBM caused by previously deposited immune aggregates instead of from deposition of newly formed immune aggregates.

Antibody nature of C3 nephritic factor. *M. R. Daha and L. A. van Es. University Hospital, Leiden, The Netherlands.* The capacity of serum from patients with membranoproliferative glomerulonephritis (MPGN) or partial lipodistrophy (PLD) to interact with normal human serum to inactivate C3 by the alternative pathway of complement activation, as assessed by loss of the B antigen of C3 was ascribed to the presence of C3 nephritic factor (C3NeF). The action of nephritic serum was magnesium-dependent and requires at least B, D, and C3. C3NeF, defined by the capacity of nephritic serum and its fractions to initiate loss of the BD, antigen of C3 in normal serum was functionally purified from the serum of five patients with MPGN and from serum of three patients with PLD, and shown to function by stabilization of the membrane-bound and fluid phase amplification convertase, C3bBb. Stabilization of C3bBb by C3NeF occurs by binding of C3NeF to the convertase. Further purification of C3NeF from nonspecific IgG was obtained by binding of C3NeF to fluid phase C3bBb, and subsequent ultracentrifugation; C3bBb (C3NeF) sediments at 10S, well separated from IgG. Highly purified C3NeF was obtained by dissociation of C3bBbC3NeF and subsequent chromatography on QAE-A50 columns. ^{125}I-C3NeF was shown to bind for at least 92% to cell-bound C3bBb, indicating conservation of functional activity. ^{125}I-C3NeF from the eight patients has a mol wt of 150,000 daltons, and is composed of two heavy and two light chains of 53,000 and 23,500 daltons, respectively. Because these data suggested that C3NeF was an IgG, its antigenic reactivity with sepharose-bound antisera was investigated. It was found that ^{125}I-C3NeF reacted with antisera against κ, λ, γ_1, γ_2, and γ_3. These results indicate that C3NeF is an immunoglobulin of the IgG class, capable of binding to C3bBb. To determine whether the Fab portion of the antibody was involved in stabilization of C3bBb, we subjected ^{125}I-C3NeF to pepsin and papain digestion, respectively. The Fab$'_2$ and Fab fragments thus generated were tested for their capacity to bind to C3bBb and to stabilize the convertase. Fab$'_2$ and Fab were four and nine times less active than was intact C3NeF to stabilize C3bBb, respectively. There was a direct relationship between the number of F(ab)$'_2$ and Fab bound to C3bBb and the rate of stabilization. These results indicate that C3NeF is an antibody of the IgG class, with specificity for the C3bBb convertase.

One year's experience with 26 high-risk patients on continuous ambulatory peritoneal dialysis. *N. Lameire, M. De Paepe, E. Matthijs, S. Ringoir. Renal Division of the Department of Internal Medicine, University Hospital, De Pintelaan, Gent, Belgium.* Our 1-year experience with 26 patients on continuous ambulatory peritoneal dialysis (CAPD) is presented. All patients were considered high-risk patients for hemodialysis because of old age, impossible vascular access, diabetes, or recent cardiovascular accidents. We used four exchanges of 2 liters each per 24 hours. Serum creatinine and blood urea at 9 months stabilized at 80% and 70% of the initial level, respectively. The use of a zero-potas-

sium dialysate resulted in hypokalemia in 5 patients requiring potassium supplements. Slight metabolic acidosis (mean plasma bicarbonate, 22 mEg/liter) was present at 9 months. We noted normal serum calcium and slightly elevated serum phosphorus, a dramatic increase in hematocrit with 6.5 volume per volume in 9 months, and a 20% fall in serum PTH at 6 months. The mean daily loss of protein in the dialysate was between 7 and 11 g, but the peritoneal creatinine clearance remained unchanged over a 9-month interval. The incidence of peritonitis was one episode per 6.3 patient-months. All episodes of peritonitis were cured with i.p. antibiotics. Sometimes dramatic deterioration of a preexisting hyperlipemia was noted in 50% of the patients. Two nondiabetic patients with plasma triglycerides over 1000 mg/dl were treated with small daily doses of crystalline insuline and responded with a 50% fall in their plasma lipids. We conclude that CAPD is an excellent alternative way of treatment of chronic renal failure in high-risk patients. We suggest that a dialysate containing 2 mEq/liter potassium and a lactate concentration of 40 mEq/liter should be available.

Successful 6-day kidney-preservation by a combination of a hypothermic continuous- and a 3-hour normothermic ex vivo perfusion: An experimental study. *B. G. Rijkmans, J. v. d. Wijk, A. J. M. Donker, M. J. H. Slooff, and G. Kootstra. Department of Surgery, State University Hospital, Groningen, The Netherlands.* The purpose of the study was to investigate the possibility of extending the preservation time of kidneys, allowing more time for advanced immunologic donor/recipient matching. In six mongrel dogs (weight, 21 to 24 kg) the right kidney was removed, flushed with a Collins-solution (4° C), and then perfused in a Gambro-preservation machine for 6 days. A 5% Kabi® albumin solution was used as perfusate. After 6 days, autotransplantation in the neck of the animal was performed, followed by contralateral nephrectomy. This series served as control for another group of six dogs, in which the period of 6 days of hypothermic machine perfusion was halfway interrupted by 3 hours normothermic ex vivo perfusion. With the animals under general anesthesia, the femoral vessels of the same animal were canulated and connected via silastic tubing with the artery and vein of the kidney that was placed in an organ chamber. In the control group, only one out of six dogs survived, versus six out of six in the ex vivo perfused group. The only survivor of the control group had a significantly higher serum creatinin concentration (maximum level, 1080 μmoles/liter on day 5) after implantation, than did the ex vivo perfused group (average maximum level, 576 μmoles/liter on day 2). These results indicate a beneficial effect of normothermic ex vivo perfusion halfway the preservation-period. In previous experiments, not presented here, we found that in our model the optimal ex vivo perfusion time was between 2 and 4 hours. During the ex vivo perfusion and 1 hour after implantation, the effective renal plasma flow (ERPF), the GFR, and the filtration fraction (FF) were calculated from clearances of ^{131}I-hippuran and ^{125}-iothalamate. The seven dogs that survived had variable values for GFR (range, 0.027 to 12 ml/min.) and ERPF (range, 0.16 to 47.48 ml/min) at 1 hour after implantation. (In this study, the value of the ERPF should not be considered as an approximation of the true renal plasma flow but rather as a measure of the proximal tubular function.) In all seven cases, however, a low FF (range, 0.07 to 0.26) was found, whereas a high FF (range, 0.52 to 1) was measured in the dogs that died. From these findings, we conclude that shortly after implantation, signs of active tubular secretion are more important than are the absolute values of GFR and ERPF. During the normothermic ex vivo perfusion, halfway the preservation period, a marked increase of the ERPF and the GFR were found, total renal blood flow being constant. The increase in ERPF was greater than was the rise in GFR, resulting in a slight decrease in FF. An increase in urine concentration was observed during the ex vivo perfusion. These data indicate an improving extraction and water resorbtion of recovering proximal tubules during the normothermic ex vivo perfusion. The results of this study will be the basis for a new experimental model, in which the animal in the ex vivo perfusion is replaced by an artificial heart-lung circuit. So, time could be provided to extend the preservation period, and, on the other hand, this system might provide the opportunity to monitor and resuscitate a damaged kidney before transplantation.

In vivo action of interferon under circumstances of immunosuppression. *W. Weimar, L. W. Stitz, A. de Reus, and H. Schellekens. Department of Internal Medicine I and Virology, Erasmus University Rotterdam, and Primate Center TNO, Virology Section, Rijswijk, The Netherlands.* Viral infections occur frequently in renal transplant recipients. One possible way to control these infections is the use of interferon. Interferons are species-specific glycoproteins with antiviral properties in vitro and in vivo. The effective prophylactic dosage of human interferon is unknown, however. Attempts to prevent viral disease in renal transplant recipients with interferon proved to be not fully successful. In a primate model, we tried to find the optimal interferon dose, and we studied the efficacy of interferon under circumstances of immunosuppression. The prophylactic antiviral activity of systemically administrated interferon was tested in 48 rhesus monkeys against vaccinia virus injected into the skin. Interferon was administred from day −1 (before vaccination) to day +7 after vaccination. *Results.* All control animals developed typical vaccinia pustulae. Human leukocyte interferon (HLI) in a dose of 5×10^5 U/kg, given i.v. and i.m., protected the monkeys completely. No lesions developed after discontinuation of therapy. Lower dosage HLI diminished lesion size. Human fibroblast interferon (HFI) in a dosage of 5×10^5 U/kg resulted in comparable efficacy as 1.25×10^5 U/kg HLI. Under immunosuppression of prednisone (6 mg/kg) and azathioprine (3 mg/kg), HLI was still active and decreased lesion size. HLI was fully active in the monkeys who received ALS (horse antihuman, 5 × 120 mg/kg): no lesions developed in these animals, but in their controls typical vaccinia pustulae were seen. *Conclusions.* Systemically administered HLI and HFI can protect rhesus monkeys against vaccinia virus. Only 5×10^5 U/kg HLI was fully effective. HLI is also active under circumstances of immunosuppression.

Protection against rejection by impaired blood flow in a renal allograft. *K. J. M. Assmann, R. A. P. Koene, R. G. W. Tiggeler, J. G. M. Rosier, and H. P. C. van Roermund. Department of Pathology and Department of Medicine, Division of Nephrology, St. Radboudziekenhuis, University of Nijmegen, The Netherlands.* Antibodies, directed against transplantation antigens, play an important role in the pathogenesis of chronic vascular rejection. The occurrence of tissue destruction is determined by the concentration of these antibodies, the density of the corresponding antigens on the allograft, and the presence of secondary mediators, like an effective complement system. Nonimmunologic factors may also be important. An observation in a patient with a renal transplant showed that the degree of perfusion is one of the factors that can extensively modify humoral rejection. A 44-year-old man received a kidney allograft for treatment of terminal renal insufficiency that was caused by an allergic vasculitis. The cadaver kidney had two arteries that were anastomosed separately to the iliac artery of the recipient. A renal biopsy taken 1 year later, showed a chronic vascular rejection. On arteriography we found a 90% stenosis in the artery that supplied the lower pole of the kidney. One half year later, renal failure had developed, and the graft was removed. After the transplantectomy, cytotoxic antibodies were demonstrable in the serum. The glomeruli in the ischemic lower pole segment did not demonstrate any sign of vascular rejection, and this was in striking contrast to the upper kidney segment. Immunoglobulin deposits and complement were found abundantly in the upper segment, but not in the lower part. The arteries in either part of the allograft had a similar degree of intimal fibrosis, but deposits of immunoglobulins and complement were not present in the vessel walls. These findings demonstrate that a reduction of the renal

perfusion in a segment of the kidney not only protects this part against a vascular rejection but also can prevent the deposition of antibodies. These antibodies were actually present in the circulation, as could be derived from the changes in the nonischemic part of the kidney and from the demonstration of circulating antibodies after removal of the graft.